



Scottish Clinical Imaging network

Scottish Clinical Imaging Network (SCIN)

SCOTTISH GUIDELINES ON THE USE OF ¹⁸F-FDG PET/CT SCANNING IN THE MANAGEMENT OF PATIENTS WITH LYMPHOMA

Scottish Clinical Imaging Network (SCIN) Scottish Guidelines on the use of ¹⁸F-FDG PET/CT Scanning in the Management of Patients with Lymphoma

Background

Guidance on the use of PET/CT scanning in patients with lymphoma was issued by SEHD in 2008 following the publication of revised response criteria and associated guidelines on the use of PET imaging in malignant lymphoma (Cheson BD et al, 2007; Juweid ME et al, 2007). The International Working Group Guidelines were revised (Cheson BD et al, 2014) and Scottish Guidance was updated in 2016 and 2020. This is a further update reflecting changes in clinical practice following BSH guidance and clinical trial results.

Most lymphomas, particularly high-grade lymphomas and Hodgkin lymphoma, are FDG avid. Small lymphocytic lymphoma, extranodal marginal lymphoma and skin lymphoma have variable FDG avidity. There is insufficient evidence and scanning capacity to permit use of this imaging modality in the staging and assessment of response in all patients with lymphoma. We have therefore limited our current recommendations to the main subtypes where management decisions may be influenced by PET/CT; Hodgkin lymphoma (HL), diffuse large B-cell lymphoma (DLBCL), T-cell lymphoma and follicular lymphoma (FL). PET/CT may be appropriate in selected patients with other lymphoma subtypes, and should be considered on a case-by-case basis in discussion with a PET radiologist.

Reporting

PET/CT response should be reported according to the Deauville criteria by radiologists/Nuclear Medicine Physicians fully trained and experienced in interpreting this imaging modality. For patients with HL, a score of 1-3 is considered negative and represents a complete metabolic response. A score of 4 or 5 is positive. However, in trials where de-escalation is based on PET response, a score of 3 may be considered an inadequate response to avoid under treatment.

Staging

PET/CT scan improves the accuracy of staging and subsequent response assessment compared to contrast CT scan. It will upstage disease in a minority of patients and may result in a change in the subsequent treatment plan. It is superior to CT scan in the identification of sites of extra nodal disease such as bone, bone marrow and liver and has replaced the need for bone marrow biopsy (BMB) in HL, and more recently in DLBCL.

Interim PET

Interim PET/CT after 2 cycles of ABVD (iPET2) is predictive of outcome in patients with advanced HL who continue on ABVD, although the optimal management of these iPET2 positive patients remains controversial. Interim PET/CT after 2 cycles of escalated BEACOPP is predictive of outcome in patients with advanced HL. Interim PET/CT scan is less predictive of outcome in patients with DLBCL and the optimal timing remains unclear and is therefore only recommended in the context of a clinical trial.

Scottish Guidelines on the use of ¹⁸F-FDG PET/CT Scanning in the Management of Patients with Lymphoma

End of treatment PET

End of treatment (EOT) PET/CT scan has high negative (94-100%) and positive (91-92%) predictive values in patients with HL and is recommended for all patients who have not achieved iPET2 negative remission as this may influence radiotherapy planning, decisions on biopsy and strategy for follow-up. However, conversion to PET negativity at EOT has no impact on prognosis in iPET2 positive patients treated with 6 cycles of ABVD.

In patients with DLBCL, end of treatment PET/CT scan has a high negative predictive value of 90-100% however the positive predictive value is lower and variable at 50-82% due to uptake in nodes post chemotherapy due to tissue inflammation and remodelling. EOT PET/CT is strongly recommended in BSH guidelines (2016) particularly in the context of residual nodes or tissue mass on conventional CT. PET avid sites should be considered for biopsy to confirm residual disease or alternatively an interval scan after 3 months (if clinically suspicion of relapse is low) is appropriate.

In patients with follicular lymphoma PET/CT is recommended for patients with apparent stage I or II disease who are being considered for curative radiotherapy. PET will identify more advanced disease in up to 60% of patients. In patients with obvious advanced stage disease PET/CT is unlikely to influence management and is not recommended. Finally, PET/CT has no currently established role in response assessment for follicular lymphoma.

Pre transplant assessment

Complete metabolic remission after salvage therapy prior to autologous transplant is highly predictive of outcome in patients with relapsed/refractory HL, DLBCL and T-cell lymphoma. Persistent PET positivity in patients treated with salvage therapy is associated with a higher risk of relapse following autologous transplant.

In general, PET/CT scans should only be performed if likely to influence management.

Scottish Guidelines on the use of ¹⁸F-FDG PET/CT Scanning in the Management of Patients with Lymphoma

Routine Indications

Hodgkin lymphoma

- Staging all patients treated with curative intent should get a baseline PET/CT scan
- Interim PET (iPET) should be performed to assess disease response to chemotherapy and guide patient management as per clinical management guidelines
- End of treatment assessment where complete metabolic response is not achieved at iPET
- Staging at relapse
- Post salvage therapy and prior to autologous transplantation

Diffuse large B-cell lymphoma (including Burkitt's lymphoma) and T-cell lymphoma

- Staging where clinically feasible
- End of treatment recommended, especially for further assessment of residual masses on CT scan
- Staging at relapse
- Post salvage therapy and prior to autologous transplantation

Follicular lymphoma

 Recommended for patients with apparent stage I or II disease on CT scan who are being considered for curative radiotherapy

CAR-T therapy

 Patients with Mantle Cell Lymphoma or DLBCL undergoing CAR-T therapy will require PET CT at baseline (pre-treatment) and during follow up at Day 28 and Day 100. Beyond this point PET CT is not routinely indicated if complete metabolic response has been achieved

Non-Routine Indications

• PET CT can be considered in other FDG avid lymphomas where the result would alter management

Future Considerations

There are many ongoing clinical trials being undertaken in the management of lymphoma. It is proposed that this guidance is reviewed on a three yearly basis in order to incorporate new evidence as it becomes available.

Scottish Guidelines on the use of ¹⁸F-FDG PET/CT Scanning in the Management of Patients with Lymphoma

References

Protocol for the use of PET scanning in patients with lymphoma (March 2008). National Guidance. <u>http://www.nhsggc.org.uk/content/default.asp?page=s1235</u>

Barnes JA et al, End-of –treatment but not interim PET scan predicts outcome in non bulky limited-stage Hodgkin's lymphoma. Ann Oncol, 22:910-915, 2011 3.

Barrington, SF et al, Establishment of a UK-wide network to facilitate the acquisition of quality assured FDG-PET data for clinical trials in lymphoma. Ann Oncol, 22:739-745, 2011

Barrington, SF et al, Role of imaging in the staging and response assessment of lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group. J Clin Oncol 32:3048-3058, 2014

Borchmann P et al. PET-guided treatment in patients with advanced-stage Hodgkin's lymphoma (HD18): final results of an open-label, international, randomised phase 3 trial by the German Hodgkin Study Group. <u>Lancet.</u> 2018, 390:2790-2802.

Chua S et al. Recommendations for cross-sectional imaging in cancer management. 2nd edition. London. The Royal College of Radiologists 2014

Cerci JJ et al, 18F-FDG PET after 2 cycles of ABVD predicts event- free survival in early and advanced Hodgkin lymphoma. J Nucl Med, 51: 1337-1343, 2010

Chaganti, S et al, Guidelines for the management of diffuse large B cell lymphoma, Br J Haem, 2016, 174, 43-56

Cheson BD et al, Revised response criteria for maligant lymphoma. J Clin Oncol, 25:579-586, 2007

Cheson BD et al, Recommendations for initial evaluation, staging and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano Classification. 32: 3059-3067, 2014

El-Galaly TC et al, Routine bone marrow biopsy has little or no therapeutic consequence for positron emission tomography/computed tomography-staged treatment-naïve patients with Hodgkin lymphoma. J Clin Oncol, 30:4508-4514, 2012

Hamilton R et al, Loss of utility of bone marrow biopsy as a staging evaluation for Hodgkin lymphoma in the positron emission tomography – computed tomography era: a West of Scotland study Leukemia & Lymphoma, 55(5):1049-1052, 2014

Gallamini A et al. The predictive role of interim positive positron emission tomography for Hodgkin lymphoma treatment outcome is confirmed using the interpretation criteria of the Deauville five-point scale. Haematologica, 99:1107-1113, 2014

Scottish Guidelines on the use of ¹⁸F-FDG PET/CT Scanning in the Management of Patients with Lymphoma

References (Cont.)

Juweid ME et al, Use of positron emission tomography for response assessment of lymphoma: Consensus recommendations of the Imaging Subcommittee of the International Harmonization project in Lymphoma. J Clin Oncol, 25:571-578, 2007

Khan AB et al, PET-CT staging of DLBCL accurately identifies and provides new insight into the clinical significance of bone marrow involvement. Blood, 122:61-67, 2013

Meignan M et al, Report on the 4th International Workshop on Positron Emission Tomography in Lymphoma. Leuk lymphoma, 55:31-37, 2014

Pregno P et al, Interim 18-FDG-PET/CT failed to predict the outcome in diffuse large B- cell lymphoma patients treated at the diagnosis with rituximab-CHOP. Blood, 119:20662073, 2012

Radford, J et al, Results of a trial of PET-directed therapy for early stage Hodgkin's lymphoma. N Engl J Med 2015; 372:1598-1607

Terasawa T et al, Fluorine-18-fluorodeoxyglucose positron emission tomography in response assessment before high dose chemotherapy for lymphoma: A systematic review and meta-analysis. Oncologist, 15:750-759,2010

Zinzani PL et al, Early interim18F-FDG PET in Hodgkin's lymphoma: Evaluation on 304 patients. Eur J Nucl Med Mol Imaging, 39:4-12, 2012